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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
| 10/621,711 | 07/17/2003 | Te-Yen Chien | AGIL-0043 | 1537 |
| 23377 7590 01/18/2007 WOODCOCK WASHBURN LLP CIRA CENTRE, 12TH FLOOR 2929 ARCH STREET PHILADELPHIA, PA 19104-2891 | | | EXAMINER GHALI, ISIS A D | |
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| | | | 1615 | |

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| SHORTENED STATUTORY PERIOD OF RESPONSE | MAIL DATE | DELIVERY MODE |
| 3 MONTHS | 01/18/2007 | PAPER |

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

| | | | |
|------------------------------|------------------------|---------------------|--|
| Office Action Summary | Application No. | Applicant(s) | |
| | 10/621,711 | CHIEN, TE-YEN | |
| | Examiner | Art Unit | |
| | Isis A. Ghali | 1615 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11/09/2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 163-174 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 163-174 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>09/05/2006</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The receipt is acknowledged of applicant's IDS filed 09/05/2006, and declarations filed 11/09/2006.

Claims 163-174 are pending and included in the prosecution.

Double Patenting

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. Claims 163-174 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-34 of U.S. Patent No. 7,045,145.

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Although the conflicting claims are not identical, they are not patentably distinct from each other because the instantly claimed subject matter is fully claimed and covered by the claims of the issued patent 7,045,145. The present claims and the claims in the issued patent are directed to common subject matter as follows: a transdermal delivery system comprising backing layer and adhesive polymer matrix layer affixed to the backing layer, wherein the adhesive polymer matrix comprising an adhesive polymer, a humectant, an estrogen, a progestin, and a combination of permeation enhancers comprising dimethyl sulfoxide, a fatty acid (C₈-C₂₀) alcohol ester of lactic acid, a lower (C₁-C₄) alkyl ester of lactic acid, and capric acid. The adhesive matrix is polyacrylate copolymer of 2-ethylhexyl acrylate and vinyl acetate and the humectant is polyvinyl pyrrolidone copolymer with vinyl acetate. The estrogen is 17- β -estradiol and progestin is levonorgestrel.

The examiner acknowledges applicants' intent to hold filling terminal disclaimer till determination of allowable subject matter.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. Claims 163-166 and 171-174 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,762,956 of ('956) in view US 5,023,084 ('084).

US '956 teaches a transdermal contraceptive delivery system comprising impermeable backing layer and adhesive matrix comprising combination of 17- β -estradiol and levonorgestrel, copolymer of 2-ethylhexyl acrylate and 3-60% of vinyl acetate, humectant, and combination of permeation enhancers comprising dimethyl sulfoxide, lauryl lactate and ethyl lactate (abstract; col.5, lines 37-60; col.6, lines 5-6, 47-48col.7, lines 50-60; col.9, lines 5-10col.16, lines 47-67).

US '956 does not teach the capric acid in the mixture of permeation enhancers.

US '084 teaches transdermal estrogen/progesterone absorption dosage unit comprising adhesive matrix comprising permeation enhancers. US '084 teaches capric acid as the preferred enhancing agent because it provides highly satisfactory skin absorption enhancement, (abstract; col.17, lines 25-57).

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide transdermal delivery device to deliver combination of estrogen and progesterone in an adhesive polymer matrix comprising combination of enhancers comprising dimethyl sulfoxide, lauryl lactate and ethyl lactate as disclosed by US '956, and further add capric acid to the adhesive combination as disclosed by US '084, motivated by the teaching of US '084 that capric acid is a preferred enhancer for estrogen and progesterone combination because it provides highly satisfactory skin absorption enhancement, with reasonable expectation of having a transdermal delivery device comprises adhesive polymer matrix comprising a combination of dimethyl

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sulfoxide, lauryl lactate, ethyl lactate and capric acid with highly satisfactory skin absorption enhancement for the combination of estrogen and progesterone.

5. Claims 167-170 are rejected under 35 U.S.C. 103(a) as being unpatentable over US '956 in view of US '084 as applied to claims 163-166 and 171-174 above, and further in view of US 6,007,835 ('835).

The teachings of US '956 and US '084 are discussed above.

However, the combination of the references does not teach polyvinyl pyrrolidone (PVP) or PVP copolymer with vinyl acetate (VA) as claimed in claims 167-170.

US '835 teaches transdermal delivery system for steroid hormones comprising and adhesive matrix comprising PVP/VA-S-630 that has content of 40% of VA and 60% PVP (abstract; col.4, lines 33-39). PVP/VA copolymer provides a matrix that exhibits the desired ergonomic and therapeutic properties, and makes it possible to obtain remarkable yield (col.6, lines 12-16). PVP/VA copolymer enhances the solubility of the hormones, and surprisingly, makes it possible to enhance the adhesion of the matrix to the skin and also causes reduction in skin irritation (col.6, lines 35-41).

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide transdermal delivery device to deliver combination of estrogen and progesterone in an adhesive polymer matrix comprising humectant and combination of enhancers comprising dimethyl sulfoxide, lauryl lactate, ethyl lactate and capric acid as disclosed by the combined teachings of US '956 and US '084, and replace the humectant by PVP/VA-S-630 copolymer disclosed by US '835, motivated by

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the teaching of US '835 that PVP/VA copolymer provides a matrix that exhibits the desired ergonomic properties with remarkable yield, enhances the solubility of the hormones, and surprisingly, makes it possible to enhance the adhesion of the matrix to the skin and also causes reduction in skin irritation, with reasonable expectation of having adhesive polymer matrix to deliver combination of hormones comprising combination of enhancers and PVP/VA-S-630 copolymer wherein the matrix exhibits the desired ergonomic properties with remarkable yield, enhances the solubility of the hormones, enhances the adhesion of the matrix to the skin and also causes reduction in skin irritation.

Response to Arguments

6. Applicant's arguments filed 11/09/2006 have been fully considered but they are not persuasive.

Applicants traverse the obviousness rejection of claims 163-166 and 171-174 over US '956 in view '084 and the obviousness rejection of claims 167-170 further in view '835 by arguing that:

- US '956 teaches only the combination of three enhancers and does not show the desirability of adding a fourth enhancer. US '084 does not teach the use of capric acid in combination with other enhancers. Therefore, no motivation to combine in the references

In response to these applicant's arguments, applicants' attention is drawn to the scope of the present claims 163-166 and 171-174 that are directed to composition, and

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all the elements of the composition are disclosed by the combined teaching of US '956 and US '084. US '956 teaches every element of the present invention except for one component of the enhancer, and this missing component is taught by US '084. US '084 teaches, unlike applicants' assertion, the use of combination of two or more enhancers that frequently provides superior results such as greater absorption of steroid hormones, col.17, lines 20-24. Also US '084 teaches that capric acid is a preferred enhancing agent for steroid hormones, col.17, lines 45-46. Therefore the art recognized the combination of enhancers and also recognized capric acid as a preferred enhancer for the steroid hormones. Additionally, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). US '956 and US '084 show that it was well known in the art at the time of the invention to use the claimed ingredients in a composition to enhance the transdermal delivery of steroid hormones. It is a *prima facie* obvious to combine two or more ingredients each of which is taught by the prior art to be useful for the same purpose in order to form a third composition which is useful for the same purpose. The idea for combining them flows logically from their having been used individually in the prior art. *In re Pinten*, 459 F.2d 1053, 173 USPQ 801 (CCPA 1972); *In re Susi*, 58 CCPA 1074, 1079-80) 440 F.2d 442, 445; 169 USPQ 423, 426 (1971); *In re Crockett*, 47 CCPA 1018, 1020-21; 279 F.2d 274, 276-277; 126 USPQ 186, 188 (1960).

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Based on the disclosure by US '956 and US '084 references that the claimed substances are used in transdermal devices as permeation enhancer for steroid hormones, an artisan of ordinary skill would have a reasonable expectation that a combination of the substances would also be useful in creating compositions to enhance transdermal delivery of steroid hormones. Therefore, the artisan would have been motivated to combine the claimed ingredients into a single composition. No patentable invention resides in combining old ingredients of known properties where the results obtained thereby are no more than the additive effect of the ingredients. See *In re Sussman*, 1943 C.D. 518; *In re Huellmantel* 139 USPQ 496; *In re Crockett* 126 USPQ 186.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide transdermal delivery device to deliver combined estrogen and progesterone in a matrix comprising combination of enhancers as disclosed by US '956, and add capric acid to the matrix as disclosed by US '084, motivated by the teaching of US '084 that the combination of enhancers containing capric acid provides highly satisfactory skin

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absorption enhancement and satisfactory adhesion and also motivated by the teaching of US '084 that capric acid is a preferred enhancer for steroid sex hormones when combination with other enhancers, with reasonable expectation of having a transdermal delivery device that comprises a combination of permeation enhancers in its matrix containing dimethyl sulfoxide, lauryl lactate, ethyl lactate and capric acid that deliver steroidal hormonal combination to the skin of the user at a satisfactory enhanced rate.

- Applicants argue that there is no teaching that would impart to the skilled artisan any reasonable expectation that combination of US '956 and US '084 would be successful.

In response to this argument, it is well established that a conclusion of obviousness under 35 U.S.C. 103 (a) does not require absolute predictability, only a reasonable expectation of success; and references are evaluated by what they suggest to one versed in the art, rather than by their specific disclosure. *In re Bozek*, 163 USPQ 545 (CCPA 1969). In considering the disclosure of the reference, it is proper to take into account not only the specific teachings of the reference but also the inferences which one skilled in the art would reasonably be expected to draw therefrom. *In re Preda*, 401 F.2d 825, 826, 159 USPQ 342, 344 (CCPA 1968). The rational to modify or to combine the prior art does not have to be expressly stated in the prior art; the rational may be expressly or impliedly contained in the prior art or it may be reasoned from knowledge generally available to one of ordinary skill in the art. It is not necessary that the prior art suggest the combination or modification to achieve the same advantage or result discovered by applicant. *In re Linter*, 458 F.2d 1013, 173 USPQ 560 (CCPA 1972).

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- Applicants argue that the addition of US '835 to support rejection of claims 167-170 is untenable in view of absence of teaching in US '956 and US '084 and does not supply suggestion to combine the cited references for teachings absent from the primary references.

Regarding this argument, it is argued that US '835 is relied upon for the solely teaching of the specific humectants in the transdermal matrices and to show that such humectants are known in the transdermal art. Further, US '835 teaches PVP/VA-S-630 copolymer provides a matrix that exhibits the desired ergonomic properties with remarkable yield, enhances the solubility of the hormones, and surprisingly, makes it possible to enhance the adhesion of the matrix to the skin and also causes reduction in skin irritation. This teaching would have motivated one having ordinary skill in the art at the time of the invention to include PVP/VA in transdermal matrices with reasonable expectation of having adhesive polymer comprising PVP/VA-S-630 copolymer wherein the matrix exhibits the desired ergonomic properties with remarkable yield, enhances the solubility of the hormones, enhances the adhesion of the matrix to the skin and also causes reduction in skin irritation. Therefore, there is

- Applicants argue that the only motivation to combine the references must have come from applicant's disclosure and not from the prior art.

In response to this argument, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of

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ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

In the light of the foregoing discussion, the Examiner's ultimate legal conclusion is that the subject matter defined by the claims would have been *prima facie* obvious within the meaning of 35 U.S.C. 103 (a).

Response to Amendment

7. The declaration of Agis Kydonieus and the declaration of Thomas Rossi under 37 CFR 1.132 filed 11/09/2006 have been considered, however, are insufficient to overcome the rejection of claims 163-174 based upon obviousness rejection under U.S.C. 103 (a) as set forth in the last Office action because:

Regarding the declaration of Agis Kydonieus:

The declaration states that US '956 is not able to deliver progestin in sufficient amount to the blood stream, and US '084 teaches multilayered matrices, unlike the present invention is a single matrix. The declaration stated that US '084 suggests range of capric acid broader than the claimed range. The declaration summarizes the improvement of the clinical results over US '956.

In response to the above statement, it is notices that US '956 disclosed and claimed that the combination of the three enhancers: dimethyl sulfoxide, lauryl lactate,

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ethyl lactate, increases progestin transdermal delivery. Regarding the disclosure of US '084, it is noticed that the present claims do not recite single matrix, and the claim language permits multilayered transdermal device. Further, no claim is made to any specific amount of capric acid. Regarding the comparison example 2 of the present invention with example 2 of US '956, it is noticed that the scope of the claims is broad covering any amounts and ratios of the four claimed enhancers while the declaration is limited to specific amount of each ingredient according to example 2. The single and specific amount of each enhancer in the composition of the declaration does not support the generic concept of the claims.

Regarding the declaration of Thomas Rossi:

The declaration shows commercial success of the product as claimed.

However, it is established that the commercial success does not support non-obviousness.

In view of the foregoing, when all of the evidence is considered, the totality of the rebuttal evidence of nonobviousness fails to outweigh the evidence of obviousness. The declaration under 37 CFR 1.132 filed 11/09/2006 is insufficient to overcome the rejection of claims 163-174 based upon obviousness under U.S.C. 103 (a) as set forth in the last Office action because it refer(s) only to the system described in the above referenced application and not to the individual claims of the application. Thus, there is

no showing that the objective evidence of nonobviousness is commensurate in scope with the claims. See MPEP § 716.

Conclusion

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Isis A. Ghali whose telephone number is (571) 272-0595. The examiner can normally be reached on Monday-Thursday, 7:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Isis A Ghali
Primary Examiner
Art Unit 1615

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